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DECLARATION UNDER 37 C.F.R. §1.132	Application Number	09/727,715
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	First Named Inventor	Garry P. Nolan
	Examiner	Teresa D. Wessendorf
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	Attorney Docket No.	RIGL-004CON

Sir:

COPY

I, Esteban Masuda, do hereby declare as follows:

I am Director of Immunology at Rigel Pharmaceuticals, Inc., the assignee of the above-captioned patent application. I have read and understood the Office Action of April 8, 2003, particularly with respect to the rejection of Claims 23-26 and 32-38 under 35 U.S.C. 101 as lacking patentable utility.

The present claims of the application are directed to libraries of biomolecules, e.g. as follows:

> A molecular library comprising at least 10^4 different retroviral nucleic acid sequences, wherein said retroviral nucleic acid sequences comprise an insertion of a nucleic acid sequence that encodes a candidate bioactive peptide of from 4 to 100 amino acids in length, wherein said candidate bioactive peptide comprises a randomized portion, and wherein each said retroviral nucleic acid sequence further comprises a sequence that encodes a reporter protein.

Based on my experience screening peptide libraries as disclosed in the present patent application, such libraries have a specific and substantial utility as research tools.

A library that meets the parameters set forth in the present claims has certain useful properties, which properties cannot be provided by a single, defined peptide. A library, as distinct from the individual components of the library, has a repertoire of binding specificities. The repertoire necessarily flows from the size, complexity, and randomization. By providing a repertoire of binding interactions, a library is useful as a research tool in investigating cell function.

It has been my observation that a library as defined by the present claims will have a repertoire sufficient to generate an informative screen for a cellular function of interest. For example, in one experiment we screened a retroviral library of random peptide 20-mers for the ability to inhibit IL-4 induced germline ε transcription using the HBEGF2a/diphtheria dual reporter phenotypic screening system described in WO 01/31232 (USSN 09/712,821). To construct the random library, A5T4 reporter cells, engineered from BJAB B-cells to reveal IL-4 induced germline ε transcription using a fluorescent reporter system, were infected with an infectious retroviral library of random peptide 20-mers (prepared as described in the present application; see also WO 01/34806 at page 39, line 36 through page 40, line 19). Cells were sorted, based on reporter expression, using a FACS. The sequences of peptides expressed by positive clones (reporter ratios of ≥1.1) were obtained by RT-PCR amplification of the integrated peptide-expressing sequences. In this experiment, of 2.4×10^9 A5T4 cells infected, 218 positive clones were identified, 199 of which were unique. Using the active peptides from this screen, several cellular proteins not previously recognized as being involved in regulation of IL-4 induced germline ε transcription were identified (*see* USSNs 10/098,243; 10/197,919; 10/197,368; 10/197,945; 10/197,962; 10/197,381; and 10/222,729).

The data presented above demonstrate that the presently claimed invention is useful as a research tool with specific, substantial utility. I am personally aware of many experiments in which molecular and cellular libraries, as described in the present claims, were used to identify transdominant peptides and cellular proteins involved in regulation of various immunological processes and cell cycle regulation. The libraries are useful in specific screening methods to identify molecular targets and biomolecules in cells, and provide a means of identifying specific compounds and targets. These utilities are distinct from the utility of a single biomolecule that interacts with a known and specific target.

I hereby declare that all statements made herein of my own knowledge are true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted,

Date: 7/7/3

By _____